

**REMARKS****Status of the Claims**

Claims 1, 3, 5-10, and 13-25 are currently pending in this application. In this response, claims 1, 3, 5-10, and 13-25 are amended to clarify the invention, and new claims 26-28 are added. Support for the amended and new claims is found throughout the specification; see, for example, US 2006/0052939 A1 at paragraphs [0022], [0024], and [0025]. No new matter has been added. Upon entry of the amendment, claims 1, 3, 5-10, and 13-28 will be pending and subject to further examination. Entry of the amendment and reconsideration on the merits in view of the following comments are respectfully requested.

**Rejection under 35 U.S.C. § 112**

Claims 1, 3, 5-10, and 13-25 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. More specifically, the Office alleges that the present specification does not provide written description for an article of manufacture configured to perform a method of reconstructing human metabolism.

As an initial matter, independent claims 1, 3, and 19 have been amended to recite “a computer-implemented method for” reconstructing metabolism of a mammalian organism in a non-disease state and a disease state (claim 1), identifying a mammalian drug target (claim 3), and predicting the existence of a novel enzyme in a mammalian organism (claim 19). As noted above, support for the amendment is found throughout the specification, for example, at paragraphs [0022], [0024], and [0025] (US 2006/0052939 A1).

Taken as a whole, the present application makes it clear that the claimed invention relates to the field of bioinformatics and thus refers to computer-implemented methods. For example, the application expressly states in paragraphs [0024] and [0025]: “Structured annotation allows the organization of heterogeneous data and the development of queries and computer algorithms that can track explicit and implicit links among these data,” and “In order to organize the information collected in the process of reconstruction, a relational database has been developed using Oracle

RDBMS.” Further, as the application explains in paragraph [0027], “By clicking the mouse on a pathway or a component of a pathway, a user can access the pathway page showing detailed diagrams with all reactions and enzymes.” Moreover, the drawings provide several examples of computer-generated pathways and networks (*see, e.g.*, Figs. 2-5). Thus, the present application clearly conveys to a skilled artisan that Applicants were in possession of a computer-implemented system capable of performing the recited method steps at the time of filing.

Accordingly, Applicants respectfully submit that this rejection under 35 U.S.C. § 112, first paragraph is rendered moot by the present amendment and may properly be withdrawn.

### **Rejection under 35 U.S.C. § 102**

Claims 1, 3, 5-10, and 13-25 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Buechler *et al.* (US 6,074,616), which allegedly discloses an article of manufacture comprising a computer readable medium having stored therein computer software (col. 22, line 5-18). Applicants traverse this rejection for the reasons set forth below.

As noted above, claims 1, 3, and 19 have been amended to recite “a computer-implemented method for” reconstructing metabolism of a mammalian organism in a non-disease state and a disease state (claim 1), identifying a mammalian drug target (claim 3), and predicting the existence of a novel enzyme in a mammalian organism (claim 19).

The legal standard for anticipation under 35 U.S.C. § 102 is one of strict identity. *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 63 U.S.P.Q.2d 1597 (Fed. Cir. 2002). “[U]nless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102.” *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed. Cir. 2008).

Buechler discloses a media carrier for a fluorescent assay device that has absolutely nothing to do with the subject matter of the present invention. As such, Buechler does not disclose any of the process steps of claims 1, 3, 5-10, and 13-25. Accordingly, Applicants respectfully submit that

the claims 1, 3, 5-10, and 13-25 as amended are not anticipated by Buechler, and therefore this rejection under 35 U.S.C. § 102 should be withdrawn.

### **Rejections under 35 U.S.C. § 103**

#### *Nakao in View of Karp and Kuffner, and further in view of Ishizuka and Takai-Igarashi*

Claims 1, 3-5, 7-10, 13, 15-20, and 22-25 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nakao *et al.* (*Genome Informatics* 1999, 10:94-103, hereinafter “Nakao”) as supported by the KEGG table of contents as of February 1999 (hereinafter “KEGG”, available at: <http://web.archive.org/web/19990203053246/www.genome.ad.jp/kegg/kegg2.html>), in view of Karp *et al.* (*Trends in Biotech.* 1999, 17:275-281, hereinafter “Karp”) and Kuffner *et al.* (*Bioinformatics*, 2000, 16(9): 825-836, hereinafter “Kuffner”), and further in view of Ishizuka *et al.* (*Inform. Process. Soc. Japan* 2000, 91:73-80, hereinafter “Ishizuka”) and Takai-Igarashi *et al.* (*In Silico Biol.* 1999, 1:129-146, hereinafter “Takai-Igarashi”).

The Office asserts that Nakao discloses a method of metabolism reconstruction for both normal and disease states, wherein data regarding a eukaryotic organism’s metabolism is collected, the data are linked to metabolic pathways, and interconnections are identified to create a map of the organism’s metabolism. The Office acknowledges that Nakao does not teach identification of drug targets. To cure this deficiency of Nakao, the Office cites Karp, which allegedly teaches that new drug targets may be identified through the analysis of pathway genome databases and that that integrated genome-metabolic pathways provide a framework for improved drug discovery. The Office further cites Kuffner, which allegedly teaches a method for combining the information found in various metabolic databases to produce a differential metabolic display (DMD), which allows the comparison between disease pathways and non-disease pathways. The Office asserts that it would have been obvious to one of skill in the art to modify the method of reconstructing an organism’s metabolism of Nakao with the drug target identification of Karp because Karp teaches that that integrated genome-metabolic pathways provide a framework for improved drug discovery. The Office further asserts that it would have been obvious to modify the method of reconstructing metabolism with collected data of Nakao and the use of pathways to identify targets of Karp with

the DMDs of Kuffner because Kuffner teaches that DMDs allow the display of significant differences in order to identify gaps in specific pathways and enable the interpretation of expression data by making predictions for proteins of unknown function and to propose the existence and/or absence of specific proteins or protein functions.

The Office also acknowledges that Nakao does not teach the creation of an interactive map. To cure this deficiency of Nakao, the Office cites Ishizuka, which allegedly discloses the construction of an interactive metabolic pathway map and teaches that the interactive map provides the advantage of presenting fundamental knowledge in biology and biochemistry. The Office asserts that it would have been obvious to one of ordinary skill in the art at the time of invention to modify the reconstruction of a mammalian, or any organism's, metabolic pathway map of Nakao, in view of Karp and Kuffner with the interactive metabolic pathway map of Ishizuka because Ishizuka allegedly shows that the interactive map provides the advantage of presenting fundamental knowledge in biology and biochemistry.

The Office further acknowledges that Nakao in view of Ishizuka does not teach that the data regarding human metabolism is exclusively used to create the interactive map. To cure this deficiency of Nakao and Ishizuka, the Office cites Takai-Igarashi, which allegedly discloses a process of reconstructing pathways, wherein data regarding human metabolism is collected in a database and used exclusively used to create the interactive map. The Office asserts that it would have been further obvious to one of ordinary skill in the art to further modify the method of metabolic reconstruction of Nakao, in view of Karp and Kuffner, and in view of Ishizuka by creating a map exclusively from human data as shown by Takai-Igarashi because Takai-Igarashi allegedly teaches that in humans metabolic pathways are more complex than other phyla such as bacteria due to the interconnections between pathways, which are considered important for the evolution of elaborate mechanisms that enable individual cells to communicate with one another to coordinate behavior for the benefit of the whole organism.

Applicants respectfully traverse this rejection for the reasons set forth below.

The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)). To establish a *prima facie* case of obviousness a three-prong test must be met. First, the prior art reference must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Second, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention. *KSR* at 1731. And third, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

As an initial matter, independent claims 1, 3, and 19 have been amended to recite an additional process step of ranking the metabolic pathways based on their relevance to human metabolism. Claims 4, 5, 7-10, 13, 15-18, 20, and 22-25 incorporate the new limitations by virtue of being dependent on claims 1, 3, and 19, either directly or indirectly. New claims 26-28 further specify what the step of metabolic pathway ranking entails.

Applicants' review of Nakao, Karp, Kuffner, Ishizuka, and Takai-Igarashi has revealed that none of these references teaches or even suggests ranking the metabolic pathways based on their relevance to human metabolism, followed by linking the ranked metabolic pathways to functional information, disease manifestations and/or high-throughput screening information. Thus, the combination of Nakao, in view of Karp and Kuffner, and further in view of Ishizuka and Takai-Igarashi, fails to disclose every element of the claimed invention. Thus, claims 1, 3-5, 7-10, 13, 15-20, and 22-25 as amended are not *prima facie* obvious, and this rejection should be withdrawn.

*Nakao in View of Karp and Kuffner, and Further in View of Ishizuka, Takai-Igarashi, and Okubo*

Claims 6, 14 and 21 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nakao as supported by KEGG, in view of Karp and Kuffner, and further in view of Ishizuka

and Takai-Igarashi, as applied to claims 1, 3-5, 7-10, 13, and 15-18 above, and further in view of Okubo *et al.* (*Nature Genetics* 1992, 2:173-179, hereinafter “Okubo”).

The Office acknowledges that Nakao in view of Karp and Kuffner, and further in view of Ishizuka and Takai-Igarashi, as applied to claims 1, 3-5, 7-10, 13, and 15-18 above, does not teach the use of EST data, as recited in the instant claims 6, 14, and 21. To cure this deficiency of Nakao, Karp, Kuffner, Ishizuka, and Takai-Igarashi, the Office cites Okubo, which allegedly teaches the use of EST data for gene mapping. The Office asserts that it would have been obvious to one of skill in the art to modify the method of metabolism reconstruction of Nakao in view of Karp and Kuffner, and further in view of Ishizuka and Takai-Igarashi, as applied to claims 1, 3-5, 7-10, 13, and 15-18 above, by incorporating the EST data of Okubo because Okubo allegedly teaches that a map of expressed genes will facilitate the search for biologically and industrially interesting genes.

Since Okubo is cited specifically for its teaching of the EST limitation, this reference does not cure the deficiencies of Nakao in view of Karp and Kuffner, and further in view of Ishizuka and Takai-Igarashi, as applied to claims 1, 3-5, 7-10, 13, and 15-18 above. Therefore, claims 6, 14, and 21 as amended are not *prima facie* obvious, and this rejection should also be withdrawn.

### **Non-Statutory Double Patenting**

Claims 3, 7 and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 and 4 of copending Application No. 11/499,437. Claims 1, 3, 5-10, 13-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 2-13 of copending Application No. 10/174,762. The Office asserts that although the conflicting claims are not identical, they are not patentably distinct from each other.

Since this is a provisional obviousness-type double patenting rejection, Applicants respectfully request that the rejection be held in abeyance until patentable subject matter is found, and that the rejection be withdrawn if it is the only remaining rejection. MPEP § 804.I.B.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 655202000300. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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